

### Remarks

This Response B is provided in response to an Office Action mailed April 22, 2003.

Applicants have amended the title of the application to be more descriptive. Applicants have added an Abstract. The objections to the claims have been corrected as suggested.

#### I Claim Rejections

Claims 1-12 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite. Applicants have amended claims 1, 2, 7 and 10 to more particularly point out the claimed invention.

Regarding claim 7, Applicants respectfully submit that the term "anti-hypertensive agent" is well understood in the art and therefore is not indefinite. According to Stedman's Medical Dictionary, 26th edition, the term "antihypertensive" is a term "indicating a drug or mode of treatment that reduces the blood pressure of hypertensive individuals." A copy of the relevant page is enclosed herewith as Appendix I. Regarding the agents that are "antihypertensive", Applicants submit that persons of ordinary skill in the medical arts can readily appreciate which compounds or drugs are antihypertensive. Applicants respectfully submit that such persons can and do refer to books such as Goodman & Gilman's The Pharmacological Basis of Therapeutics, Ninth Edition (1996) for discussion of antihypertensive agents. In particular, Chapter 33, entitled Antihypertensive Agents and the Drug Therapy of Hypertension includes numerous examples of such agents and their uses. Applicants submit that such textbooks as well as others are well known in the art and need not be cited.

Claim 8 has been amended to make explicit the end point that was inherent in the preamble of the claim. Further, Applicants submit that the term "effective concentration" of an agent used to treat a condition is a concentration that actually affects the condition. Thus, if a goal of therapy is to create an anti-hypertensive effect, an "effective concentration" is a concentration that causes an anti-hypertensive effect (vis. lowers blood pressure). Applicants submit that measurement of blood pressure is a common technique, and the particular methods or criteria used need not be

explicitly disclosed in the claims. Thus, Applicants submit that the term "effective concentration" will be well understood by persons of ordinary skill in the art.

All of the other claims subject to this rejection depend from at least one of the claims discussed immediately above. Insofar as the independent claims are not indefinite, and the other terms used are not indefinite, Applicants submit that the claims depending therefrom are also not indefinite, and Applicants respectfully request reconsideration of the rejections and find the claims allowable.

## II. Rejections Under 35 U.S.C. §103

Claims 1-12 stand rejected under 35 U.S.C. §103, as obvious over Barker in view of Job and Coves.

Applicants submit that there has been no *prima facie* case for obviousness made. To make a *prima facie* case for obviousness of a combination of references, there has to be a reasonable expectation of success of arriving at the Applicants' claims based on the teachings of the references and what is well known in the art.

The Examiner cited Barker for the teaching of a relationship between fetal programming and elevated blood pressure. However, Barker did not teach any causal link between fetal programming and elevated blood pressure. Barker did not teach or suggest any effect of growth hormone. As the Examiner stated: "Barker et al. do not explicitly recite the administration of GH to treat hypertension in a mammal..." Office action, page 5, end of first paragraph. Applicants note that Barker did not discuss any aspect of growth hormone in relation to fetal programming or elevated blood pressure.

Additionally, the Examiner cited Job for the teaching of a relationship between growth hormone administration and accelerated growth in affected children of low birth weight. Job

Finally, the Examiner cited Coves for the teaching of an observation of dual effects of guanfacine, a centrally acting  $\alpha$ -adrenergic agonist, to increase growth hormone levels and to decrease blood pressure in patients with diabetes. Coves did not, however, teach or suggest a causal link between growth hormone and reduction in blood pressure in any subject. Although the Examiner stated "Coves et al. teaches the effect of GH on blood pressure of patients with hypertension," Applicants' reading of Coves does not support that conclusion.

Applicants respectfully submit that Coves' findings could reasonably reflect two, independent effects of the drug used (i.e. increased growth hormone levels and decreased blood pressure), and that the findings do not teach a direct, causal link between increased growth hormone levels and decreased blood pressure. Coves did not disclose any results in which growth hormone was administered to any patient with hypertension. Further, Applicants also submit that Coves provides no teaching or suggestion that the dual effects observed in diabetic patients could be generalized to other subjects, such as those subjected to fetal programming. In fact, Coves explicitly teaches away from such a generalization. "...[I]t is shown that the oral administration of guanfacine to hypertensive subjects does not modify plasma GH levels." Page 292. Thus, Applicants submit that Coves cannot form a reasonable basis to believe that guanfacine modifies GH levels in mammals subject to fetal programming.

Applicants respectfully submit that, based upon Barker, Job and Coves and what is reasonably known in the art, there is no teaching or suggesting of (1) a direct link between growth hormone and decreased blood pressure, or (2) a use of growth hormone for therapeutic treatment for hypertension. The only reference that teaches the use of GH for any purpose is Job, which does not directly address any issue relating to blood pressure, and does not provide any teaching of a relationship between GH and fetal programming. None of the other cited art in combination or separately provide the necessary teaching to render the Applicants' claims obvious. Applicants submit that at best, there may be an "invitation to experiment" based on the combination of the three cited references. An invitation to experiment is not sufficient to provide a reasonable expectation of success at arriving at the Applicants' invention, and thus cannot be the basis for a *prima facie* case of obviousness.

In contrast to the lack of teaching by the combination of Barker, Job and Coves, Applicants respectfully submit that it was the Applicants' disclosure that provided the link between growth hormone administration and decreased blood pressure in mammals subject to fetal programming. Experimental evidence is presented throughout the specification specifically disclosing the use of growth hormone to decrease blood pressure in mammals subjected to fetal programming.

Thus, it is the instant invention bridges the gaps in the art by demonstrating, for the first time, that there is a direct relationship between increasing growth hormone

levels and achieving a reduction in blood pressure in mammals subject to fetal programming. Applicants respectfully suggest that the rejections under 35 U.S.C. §103 are hindsight reconstructions based on the Applicants' disclosure. As such, Applicants respectfully submit that there has not been a *prima facie* case presented for obviousness.

Based on the arguments presented herein, Applicants respectfully request the Examiner to reconsider the rejections and find the claims allowable. Additionally, Applicants respectfully request the Examiner to examine the newly added claims in light of the above discussion and to find those claims allowable. If the Examiner believes that a discussion with the undersigned Attorney would be helpful in addressing these issues, the undersigned invites the Examiner to call at the telephone number below.

The Commissioner is authorized to charge any underpayment or credit any overpayment to Deposit Account No. 06-1325 for any matter in connection with this response, including any fee for extension of time, which may be required.

Respectfully submitted,

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By: 

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